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The Impact of Postoperative Complications on Long-term Oncologic Outcomes After Laparoscopic Low Anterior Resection for Rectal Cancer

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Abstract: Laparoscopic rectal cancer surgery has technical difficulties with a higher complication rate than colon cancer. However, few studies have examined whether postoperative complications are associated with oncologic outcomes. The aim of this study is to evaluate the impact of postoperative complications on long-term oncologic outcomes after laparoscopic low anterior resection for rectal cancer.

Between January 2005 and December 2012, we evaluated 686 consecutive patients who underwent laparoscopic low anterior resection for stage I-III rectal cancer. Patients were divided into complication (n = 175) and noncomplication (n = 511) groups. The median follow-up period was 38 months (range, 2–118). We compared perioperative clinicopathologic outcomes, 5-year survival, and local recurrence between groups and evaluated prognostic factors.

Five-year overall survival rates were 91.4% and 89.2% ($P = 0.234$) and 5-year disease-free survival rates were 83.2% and 77.7% ($P = 0.002$) in the noncomplication and complication groups for all stages, respectively. For stage I cancer, both the 5-year overall survival and the 5-year disease-free survival rate of the complication group were lower than the noncomplication group. Local recurrence rates were 3.1% and 7.8% in the noncomplication and complication groups, respectively ($P = 0.002$). In multivariate analysis, the presence of postoperative complications was a significant predictor of 5-year disease-free survival (hazard ratio, 1.65; $P = 0.012$).

Postoperative complications had a negative impact on 5-year disease-free survival after laparoscopic low anterior resection for rectal cancer. The rate of local recurrence in the complication group increased more than the noncomplication group. In particular, postoperative complications were associated with poorer oncologic outcomes for stage I cancer. Laparoscopic surgery is preferred for early-stage rectal cancer so careful attention should be paid to avoid postoperative complications.

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Abbreviations: ASA = the American Society of Anesthesiologists, BMI = body mass index, CG = complication group, CRM = circumferential resection margin, GPS = Glasgow prognostic score, HR = hazard ratio, LAR = low anterior resection, NCG = non-complication group, POSSUM = Physiology and Operative Severity Score for enUmeration of Mortality and morbidity, SIR = systemic inflammatory response, TNM = tumor node metastasis.

INTRODUCTION

Laparoscopic surgery is regarded as a safe and feasible procedure for colorectal cancer. Randomized controlled trials and meta-analyses comparing laparoscopic surgery with open surgery have reported similar long-term oncologic outcomes for the 2 procedures.[1–5] However, laparoscopic surgery has been reported to be associated with a shorter hospital stay, less pain, and similar postoperative complication rates than open surgery.[6,7] In addition, laparoscopic surgery is a technically advanced procedure with features that include a magnified view, which facilitates meticulous dissection in cases of rectal cancer surgery.

Laparoscopic surgery has been shown to be associated with higher complication rates when performed for rectal cancer than when performed for colon cancer because of technical difficulties and anatomical limitations in the pelvic cavity. According to the results of the CLASICC trial, the complication rate for rectal surgery was 13%, higher than the 7% rate for colon surgery.[8] In addition, the anastomotic leakage rate was higher for rectal surgery (10.2%) than for colon surgery (2.3%; $P < 0.001$).[9] Furthermore, postoperative morbidities could delay the administration of adjuvant therapy, increase hospital stay, and reduce cost-effectiveness.[10,11]

Previous studies on laparoscopic rectal cancer surgery focused on feasibility and safety in terms of oncologic outcomes compared with those for open rectal cancer surgery. Few studies have examined whether postoperative complications are associated with oncologic outcomes following laparoscopic colorectal surgery. Therefore, we aimed to evaluate the impact of postoperative complications on the long-term oncologic outcomes after laparoscopic low anterior resection (LAR) for rectal cancer.

METHODS

Study Population and Data Collection

Between January 2005 and December 2012, 686 consecutive patients underwent laparoscopic LAR for stage I-III rectal cancer at Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea. Because the focus of this study was the laparoscopic procedure, patients who underwent open or robotic surgery were excluded. In addition, patients who had colon cancer or carcinoid tumors were not included. Patients who underwent abdominoperineal resection were also

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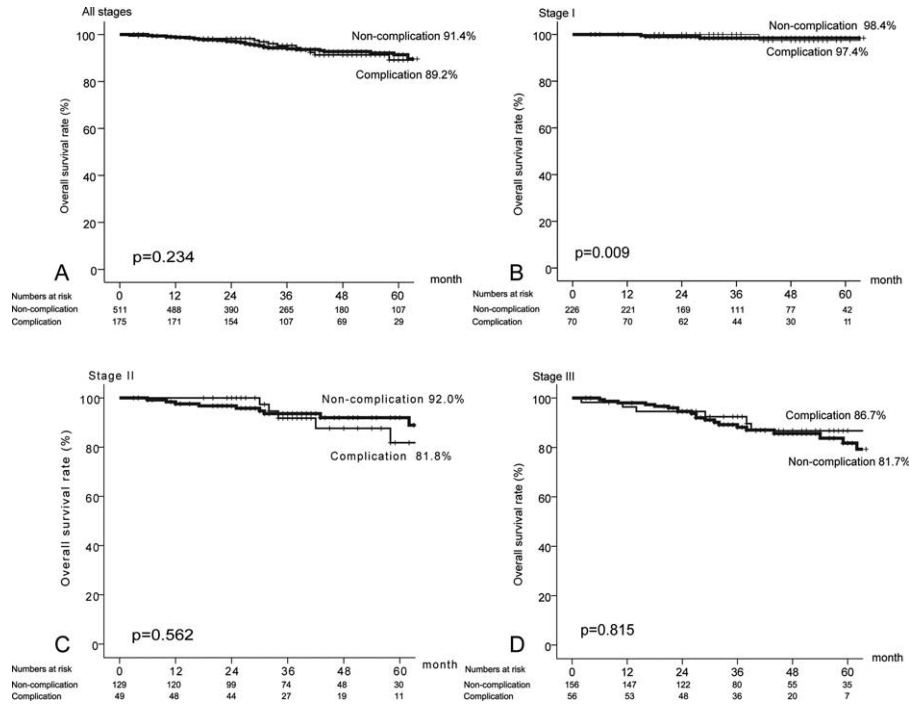

FIGURE 1. Five-year overall survival rates: A, All stages; B, Stage I; C, Stage II; D, Stage III.

excluded, because the different surgical procedures used for the perineal wound could confound postoperative outcomes. Seven patients who were lost to follow-up and 6 who died within 1 month after surgery (postoperative mortality cases) were excluded. Finally, 686 patients were divided into 2 groups according to the occurrence of postoperative complications: the complication group (CG, n = 175) and the noncomplication group (NCG, n = 511).

All data were collected from the Yonsei Colorectal Cancer Database, and data completeness was ensured by electronic medical chart review and telephone interviews. This study was approved by the Institutional Review Board of Severance Hospital.

Evaluation Parameters

The patients were divided into 2 groups (CG and NCG) and were evaluated for the following parameters: age, sex, weight, height, body mass index (BMI), and the American Society of Anesthesiologists (ASA) classification.

Tumor location was classified as low ($\leq$5 cm), mid (5.1–10 cm), or upper rectal (10.1–15 cm), according to the tumor's distance from the anal verge. Patients who had undergone abdominal surgery before the rectal cancer surgery were considered to have a history of abdominal surgery.

The perioperative outcomes evaluated operation time and the amount of intraoperative bleeding. Diverting ileostomy was performed in patients with a high risk of postoperative leakage (male patients with mid/low rectal cancer and patients who received preoperative chemoradiotherapy), a positive air-leak test, or a hand-sewn colo-anal anastomosis. The criterion for conversion to open surgery was an unintended extension (by more than 4 cm) of the incisional site during surgery. Length of hospital stay was calculated from the date of surgery to the date of discharge.

Pathologic outcomes were assessed according to the tumor node metastasis (TNM) stage (American Joint Committee on Cancer, seventh edition).[12] On the basis of histologic findings, tumors were considered to have a well, moderate, poor, or mucinous differentiation. The surgical specimen was analyzed to determine the number of harvested lymph nodes, lymphovascular invasion, and the circumferential resection margin (CRM). CRM involvement was defined as the presence of tumor cells within 1 mm of the CRM.[13] Tumor size, the proximal resection margin, and the distal resection margin were determined in the operating room, and pathologic reports were reviewed to obtain additional information.

The oncologic outcomes were evaluated by overall survival, disease-free survival, and local recurrence. Overall survival was calculated from the date of surgery to the date of death. Disease-free survival was calculated from the date of surgery to the date of death or recurrence. Local recurrence was defined when recurrence was observed at the primary site on radiologic or histologic examination. Recurrence beyond the primary site was considered to be distant metastasis. Five-year survival rates were compared between the CG and NCG.

Postoperative Complications and Their Grading

Complications that occurred after surgery were considered to be postoperative complications. These were classified according to the Clavien-Dindo classification as summarized in Table 3.[14] In cases of multiple complications in a patient, the one with the highest Clavien-Dindo classification was recorded for analysis. We then compared oncologic outcomes between patients with grade I-II complications and those with grade III-IV complications (Figure 1).

Neoadjuvant Therapy and Postoperative Surveillance

Patients with T3/4 mid or low rectal cancer or positive lymph nodes were treated with preoperative chemoradiotherapy

TABLE 1. Patient Characteristics

	Noncomplication Group (n = 511)	Complication Group (n = 175)	*P*
Age (years)	62.0 ± 10.3 (28–87)	62.4 ± 10.2 (31–89)	0.602*
Sex			0.001†
Male	295 (57.7)	126 (72.0)	
Female	216 (42.3)	49 (28.0)	
Weight (kg)	61.1 ± 9.5 (36–87)	63.7 ± 10.6 (43–94)	0.003*
Height (cm)	161.9 ± 8.6 (140–184)	164.2 ± 8.9 (135–182)	0.003*
BMI (kg/m^2)	23.3 ± 3.0 (14.5–38.0)	23.6 ± 3.3 (16.7–34.9)	0.234*
ASA score			0.640†
1	215 (42.1)	67 (38.3)	
2	282 (55.2)	102 (58.3)	
3	14 (2.7)	6 (3.4)	
Tumor location from anal verge			0.224†
Low (0–5 cm)	87 (17.0)	34 (19.4)	
Mid (5.1–1 0cm)	276 (54.0)	102 (58.3)	
High (10.1–15 cm)	148 (29.0)	39 (22.3)	
History of abdominal surgery			0.029†
Yes	77 (15.1)	15 (8.6)	
No	434 (84.9)	160 (91.4)	
Preoperative chemoradiotherapy			0.086†
Yes	124 (24.3)	54 (30.9)	
No	387 (75.7)	121 (69.1)	

Continuous variables are described as mean ± standard deviation (range); categorical variables are described as n (%).
ASA = American Society of Anesthesiologists, BMI = body mass index.
*Student *t* test.
†Chi-square test.

(50.4 Gy in 28 fractions for a total radiotherapy dose and 5-fluorouracil or a capecitabine-based regimen). Surgery was performed within 6 to 8 weeks after the completion of preoperative chemoradiotherapy. If preoperative chemoradiotherapy was not possible, postoperative chemoradiotherapy was administered.

Patients visited the outpatient clinic every 3 months thereafter for the first 2 years, and then, every 6 months until 5 years postoperatively. Chest and abdominopelvic computed tomography were performed every 6 months, and regular laboratory test results, including those for carcinoembryonic antigen, were examined at every visit. According to the National Comprehensive Cancer Network guidelines, all patients with stage III rectal cancer and those with stage II cancer and high-risk factors received 5-flourouracil based adjuvant chemotherapy.

Surgical Technique

Laparoscopic LAR was performed by high ligation of the inferior mesenteric vessel, left colon mobilization, and splenic flexure mobilization. Pelvic dissection was performed according to the principles of total meseorectal excision.[15] The avascular plane between the presacral fascia and proper fascia of the rectum was dissected. The specimen was extracted through a mini-laparotomy, 3 to 4 cm from the trocar site in the lower left quadrant area. After inserting an end-to-end anastomosis (EEA) anvil into the proximal colon, intracorporeal anastomosis between the proximal colon and distal rectum was performed using the double-stapling method and hand-sewn colo-anal anastomosis. For colo-anal anastomosis, dissection of the rectum was reached at the level of the dentate line. After resecting the tumor, anastomosis between the anal canal at the level of the dentate line and proximal colon was performed.

Statistical Analysis

Statistical analysis was performed with SPSS v. 20 for Windows (SPSS Inc., Chicago, IL). Categorical variables were analyzed using the Chi-square test or Fisher exact test. Continuous variables were analyzed using the Student *t* test. The 5-year overall survival, 5-year disease-free survival, and local recurrence rates were evaluated using the Kaplan-Meier method. Comparisons of 5-year survival and local recurrence between the CG and NCG were made using the log-rank test. Univariate analysis to identify prognostic factors affecting 5-year survival was performed using the log-rank test. Variables found to be significant in univariate analysis were entered into the Cox proportional hazards regression model for multivariate analysis. A *P* value less than 0.05 was considered statistically significant for all parameters.

RESULTS

Patient Characteristics

Patient characteristics were compared between the CG and NCG. The proportion of men was higher in the CG than in the NCG (72.0% vs 57.7%, $P = 0.001$). Height and weight values were also higher in the CG than in the NCG. However, BMI was not significantly different between the 2 groups ($P = 0.234$). The rate of a history of abdominal surgery was higher in the NCG (15.1%) than in the CG (8.6%; $P = 0.029$). Age, the ASA score, and the administration of preoperative chemoradiotherapy did not differ significantly between the groups. The distributions of tumor location were not significantly different ($P = 0.224$); mid-rectal cancers, located 5.1 to 10 cm from the anal verge, were the most common in both groups (Table 1).

TABLE 2. Perioperative and Pathologic Outcomes

	Noncomplication Group (n = 511)	Complication Group (n = 175)	*P*
Operation time (min)	250.9 ± 82.2 (66–664)	292.8 ± 177.5 (98–2270)	0.003*
Intraoperative bleeding (mL)	124.4 ± 210.9 (0–1550)	187.6 ± 287.8 (0–2300)	0.008*
Anastomotic type			0.132‡
Double stapling method	464 (90.8)	150 (85.7)	
Colo-anal J-pouch	5 (1.0)	2 (1.2)	
Colo-anal-straight	42 (8.2)	23 (13.1)	
Diverting ileostomy			0.463†
Yes	140 (27.4)	53 (30.3)	
No	371 (72.6)	122 (69.7)	
Conversion			0.011‡
Yes	6 (1.2)	8 (4.6)	
No	505 (98.8)	167 (95.4)	
Length of hospital stay (days)	9.1 ± 4.2 (4–49)	16.1 ± 13.2 (5–92)	<0.001*
TNM stage			0.603†
I	226 (44.2)	70 (40.0)	
II	129 (25.3)	49 (28.0)	
III	156 (30.5)	56 (32.0)	
Histologic differentiation			0.206‡
Well	134 (26.2)	35 (20.0)	
Moderate	358 (70.1)	137 (78.3)	
Poor	7 (1.4)	1 (0.6)	
Mucinous	12 (2.3)	2 (1.1)	
Numbers of harvested lymph nodes	15.7 ± 7.7 (3–49)	16.4 ± 8.8 (3–49)	0.340*
Tumor size (cm)	3.0 ± 1.8 (0.1–11.2)	3.1 ± 1.9 (0.1–10.0)	0.548*
Proximal resection margin (cm)	12.2 ± 5.0 (5.0–35.0)	12.5 ± 4.9 (5.0–30.0)	0.427*
Distal resection margin (cm)	2.6 ± 1.9 (0.1–12.0)	2.4 ± 1.5 (0.1–7.0)	0.110*
Lymphovascular invasion	76 (14.9)	31 (17.7)	0.371†
CRM			0.182†
Noninvolved (>1 mm)	480 (93.9)	169 (96.6)	
Involved (≤1 mm)	31 (6.1)	6 (3.4)	

Continuous variables are described as mean ± standard deviation (range); categorical variables are described as n (%).
CRM = circumferential resection margin, TNM = tumor node metastasis.
*Student *t* test.
†Chi-square test.
‡Fisher exact test.

Perioperative and Pathologic Outcomes

With respect to perioperative outcomes, operation time was longer in the CG than in the NCG (292.8 ± 177.5 vs 250.9 ± 82.2 min, $P = 0.003$). The amount of intraoperative bleeding was greater in the CG than in the NCG (187.6 ± 287.8 vs 124.4 ± 210.9 mL, $P = 0.008$). Conversion to open surgery was significantly more frequent in the CG than in the NCG (4.6% vs 1.2%, $P = 0.011$). The length of hospital stay was longer in the CG than in the NCG (16.1 ± 13.2 vs 9.1 ± 4.2 days, $P < 0.001$). However, anastomosis type and the rate of diverting ileostomy were not significantly different between groups.

With respect to pathologic outcomes, there were no significant differences for any of the parameters. The distributions of TNM stage did not differ between the groups ($P = 0.603$). Histologic differentiation, number of harvested lymph nodes, tumor size, lymphovascular invasion, and proximal and distal resection margins also did not differ significantly between the 2 groups. The rates of CRM involvement were 3.4% in the CG and 6.1% in the NCG, but this difference was not significant ($P = 0.182$), as summarized in Table 2.

Postoperative Complications According to Their Clavien-Dindo Classification

Postoperative complications according to their Clavien-Dindo classification are listed in Table 3. The overall rate of postoperative complications was 25.4%. Of these, 6.3% were grade I complications. Voiding difficulty was the most common complication (3.5% of the patients), and ejaculation dysfunction was the second most common complication. In total, 2.6% of the patients had grade II complications that included intestinal obstruction (1.2%), ischemic colitis (0.3%), perianal abscess (0.1%), wound infection (0.1%), and anastomotic leakage (0.9%), which were treated by antibiotics. Overall, 1.7% of the patients had grade IIIa complications, and anastomotic stricture, which was treated by endoscopic balloon dilatation, was the most common complication among these. The rate of grade IIIb complications was 14.4%. Anastomotic leakage was the most common grade IIIb complication (7.0%) and intestinal obstruction was the second most common (3.1%). Nine patients had rectovaginal fistulas and 1 had a rectovesical fistula. There were 8 patients, who were treated by a diverting loop ileostomy

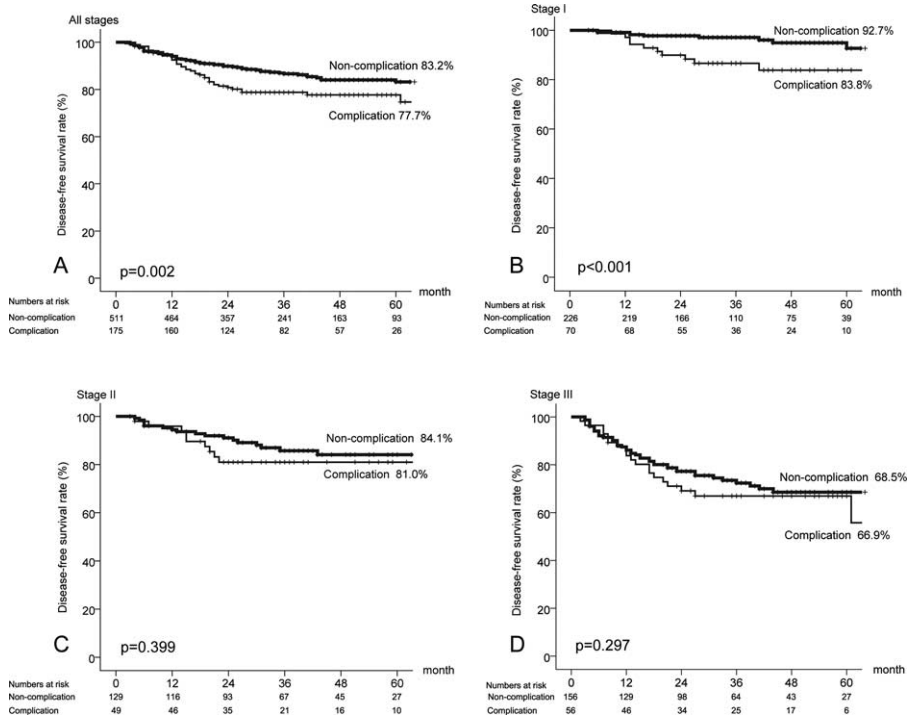

FIGURE 2. Five-year disease-free survival rates: A, All stages; B, Stage I; C, Stage II; D, Stage III.

(0.9%) or a colostomy formation (0.4%) due to anastomotic stricture. One patient with fecal incontinence underwent a diverting ileostomy, and the complication was classified as grade IIIb. Three patients had grade IV complications, which included pneumonia, strangulation of the intestine, and stress-induced cardiomyopathy.

Oncologic Outcomes in the CG and NCG

The mean follow-up period was 43.6 ± 0.9 months (interquartile range, 26–58 months), and the median follow-up period was 38 months (range, 2–118 months). As shown in Figure 2, the 5-year overall survival rate for all stages was not significantly different in the CG and NCG (89.2% and 91.4%, respectively; $P = 0.234$). However, for stage I cancer, the 5-year overall survival rate was significantly higher in the NCG than in the CG (98.4% vs 97.4%, $P = 0.009$). The proportions of patients with stage II and III cancer were not significantly different between the groups, as shown in Figure 2.

The 5-year disease-free survival rate for all stages was significantly different between the CG and NCG as described in Figure 3 (77.7% vs 83.2%; $P = 0.002$). In addition, for stage I cancer, the 5-year disease-free survival rate was significantly lower in the CG (83.8%) than in the NCG (92.7%, $P < 0.001$). There were no significant differences between groups in the 5-year disease-free survival rates for patients with stage II and III cancer (Figure 3).

The cumulative incidence of local recurrence was higher in the CG than in the NCG (7.8% vs 3.1%, $P = 0.002$), as shown in Figure 4.

We compared oncologic outcomes between patients with grade I-II complications and patients with grade III-IV complications according to the Clavien-Dindo classification of surgical complications, as described in Figure 1.[14] The 5-year disease-free survival rate among patients without postoperative complications was 91.9%. Patients with postoperative complications had a lower 5-year disease-free survival, which was 91.5% for grade I-II complications and 72.1% for grade III-IV complications ($P < 0.001$). However, 5-year overall survival did not differ significantly according to the grade of postoperative complications.

Prognostic Factors for the 5-year Survival Rate

In univariate analysis, age, conversion to open surgery, TNM stage, histologic differentiation, number of harvested lymph nodes, lymphovascular invasion, and postoperative complications were prognostic factors for 5-year disease-free survival. With respect to 5-year overall survival, age, conversion to open surgery, TNM stage, histologic differentiation, lymphovascular invasion, and CRM involvement were prognostic factors (Table 4). Thus, age, conversion to open surgery, TNM stage, histologic differentiation, and lymphovascular invasion were the common prognostic factors for 5-year overall survival and 5-year disease-free survival.

In multivariate analysis, TNM stage, number of harvested lymph nodes, and postoperative complications were found to be prognostic factors for 5-year disease-free survival. The hazard ratio (HR) was lower for $\geq$12 harvested lymph nodes than for $<$12 harvested lymph nodes ($\geq$12 vs $<$12, HR, 0.52; $P = 0.001$). The HR for 5-year disease-free survival was higher in the CG than in the NCG (HR, 1.65; $P = 0.012$). The prognostic factors for 5-year overall survival were age, TNM stage, and histologic differentiation in multivariate analysis. TNM stage was a common prognostic factor for 5-year disease-free survival and 5-year overall survival. Compared with patients with stage I cancer, the HR for disease-free survival among patients with stage III rectal cancer was 3.88 ($P < 0.001$) and

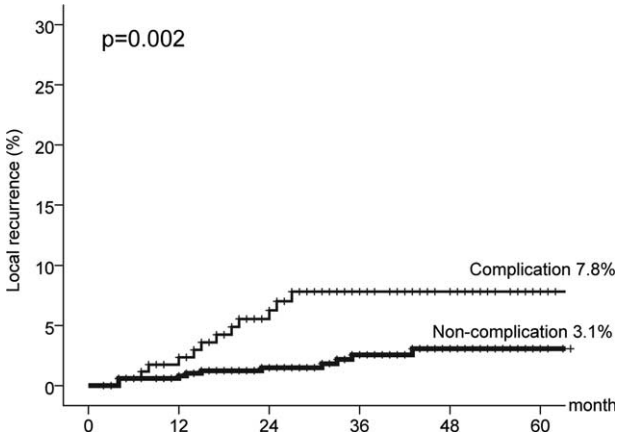

FIGURE 3. Cumulative incidence of local recurrence.

that for overall survival was 3.27 ($P = 0.006$). However, the occurrence of postoperative complications was only the prognostic factor for 5-year disease-free survival (Table 5).

DISCUSSION

In this study, we investigated whether postoperative complications after laparoscopic LAR influence long-term oncologic outcomes in patients with rectal cancer. The most important finding was that patients in the NCG with stage I cancer had higher rates of both 5-year disease-free survival and overall survival than those in the CG. In addition, although there was no significant difference in the 5-year overall survival between the CG and NCG for all stages ($P = 0.234$); the 5-year disease free survival rate was higher and the local recurrence rate was lower in the NCG than in the CG. The pathologic parameters related to cancer behavior were not found to be confounding factors in the interpretation of the present results, because there were no significant differences between the CG and NCG in terms of TNM stage, histologic differentiation, tumor size, resection margins, lymphovascular invasion, and CRM involvement.

Oncologic outcomes were not significantly different between the CG and NCG for patients with stage II and III rectal cancer. These results suggest that postoperative complications did not influence oncologic outcomes in patients with stage II or III rectal cancer. However, for stage I rectal cancer, oncologic outcomes were poorer in the CG than in the NCG. Thus, in the early stages of rectal cancer, postoperative complications may affect oncologic outcomes in the absence of pathologic tumor infiltration into perirectal fat or lymph node metastasis. Meanwhile, the effect of postoperative complications on oncologic outcomes might be diluted in patients with stage II-III rectal cancer because of the relatively higher pathologic stage and tumor aggressiveness than in patients with stage I rectal cancer. These results are supported by the fact that excessive systemic inflammatory responses (SIRs) due to

TABLE 3. Details of Postoperative Complications

Postoperative Complications	Case No. (%)
Grade I	43 (6.3%)
Voiding difficulty	24
Ejaculation dysfunction	9
Urinary frequency	5
Fecal incontinence	1
Dysuria	1
Wound seroma	1
Wound dehiscence	2
Grade II	18 (2.6%)
Intestinal obstruction	8
Ischemic colitis	2
Perianal abscess	1
Wound infection	1
Anastomotic leakage	6
Grade IIIa	12 (1.7%)
Anastomotic site stricture	7
Intestinal obstruction	3
Anastomotic site bleeding	1
Presacral abscess	1
Grade IIIb	99 (14.4%)
Anastomotic leakage	48
Anastomotic site stricture	8
Intestinal obstruction	21
Incisional hernia	7
Presacral abscess	2
Rectovaginal fistula	9
Rectovesical fistula	1
Vesicocutaneous fistula	1
Anastomotic site bleeding	1
Fecal incontinence	1
Grade IV	3 (0.4%)
Aspiration pneumonia	1
Strangulation of intestine	1
Stress-induced cardiomyopathy	1

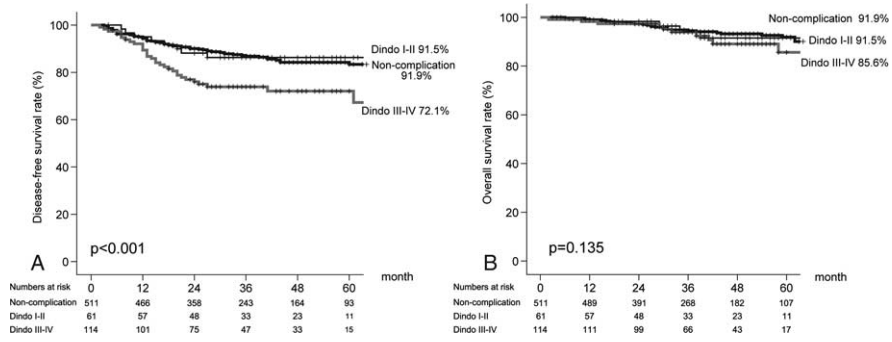

FIGURE 4. Five-year survival according to Clavien-Dindo classification of postoperative complications: A, Five-year disease-free survival rate; B, Five-year overall survival rate.

TABLE 4. Prognostic Factors for 5-year Survivals by Univariate Analysis

	No. (n = 686)	DFS (%)	*P*	OVS (%)	*P*
Age (years)			0.013		0.001
≤65	409	84.2		94.1	
>65	277	78.1		85.7	
Sex			0.284		0.364
Male	421	80.1		89.6	
Female	265	84.3		92.7	
BMI (kg/m^2)			0.178		0.845
≤25	507	80.5		90.9	
>25	179	85.1		90.6	
ASA score			0.809		0.838
ASA 1∼2	666	81.5		90.5	
ASA ≥3	20	89.5		100.0	
Tumor location from anal verge			0.400		0.070
Low (0–5 cm)	121	81.6		94.1	
Mid (5.1–10 cm)	378	79.5		86.6	
High (10.1–15 cm)	187	85.9		95.7	
Preoperative chemoradiotherapy			0.750		0.307
Yes	178	84.3		95.6	
No	508	81.2		89.9	
Operation time (min)			0.500		0.938
≤265	393	83.6		90.7	
>265	293	79.6		91.0	
Anastomotic type			0.855		0.446
Double stapling method	614	81.8		90.2	
Colo-anal J-pouch	7	80.0		100.0	
Colo-anal-straight	65	83.0		95.5	
Diverting ileostomy			0.495		0.776
Yes	193	77.2		89.0	
No	493	83.1		91.0	
Conversion			0.030		0.022
Yes	14	64.3		84.4	
No	672	82.1		91.2	
TNM stage			<0.001		<0.001
I	296	90.4		98.1	
II	178	83.1		89.0	
III	212	68.3		83.0	
Histologic differentiation			<0.001		<0.001
Well	169	88.6		95.9	
Moderate	495	80.4		90.1	
Poor	8	62.5		32.8	
Mucinous	14	65.5		72.9	
Number of harvested lymph nodes			0.002		0.111
<12	211	73.9		88.4	
≥12	475	85.9		92.1	
Lymphovascular invasion			0.001		0.002
Yes	107	71.4		82.8	
No	579	83.7		92.4	
CRM			0.129		0.030
Noninvolved (>1 mm)	649	82.3		91.1	
Involved (≤1 mm)	37	72.6		85.4	
Postoperative complications			0.002		0.234
Yes	175	77.7		89.2	
No	511	83.2		91.4	

CRM = circumferential resection margin, DFS = disease-free survivals, OVS = overall survivals, TNM = tumor node metastasis.

TABLE 5. Prognostic Factors for 5-year Survivals by Multivariate Analysis

	Disease-free Survivals		Overall Survivals	
	HR (95% CI)	P^*	HR (95% CI)	P^*
Age (years)		0.137		0.004
>65 vs ≤65	1.33 (0.91–1.94)		2.33 (1.31–4.14)	
Conversion		0.051		0.069
Yes vs no	2.48 (1.00–6.18)		2.72 (0.93–8.01)	
TNM stage		<0.001		0.023
II vs I	1.81 (1.01–3.23)	0.046	2.13 (0.87–5.24)	0.099
III vs I	3.88 (2.31–6.50)	<0.001	3.27 (1.39–7.67)	0.006
Histologic differentiation		0.162		0.012
Moderate vs well	1.62 (0.91–2.86)	0.101	1.97 (0.80–4.86)	0.141
Poor vs well	3.32 (0.93–11.89)	0.065	11.74 (2.66–51.72)	0.001
Mucinous vs well	2.34 (0.80–6.90)	0.122	2.58 (0.58–11.42)	0.211
Number of harvested lymph nodes		0.001		
≥12 vs <12	0.52 (0.35–0.76)			
Lymphovascular invasion		0.675		0.407
Yes vs no	1.10 (0.70–1.73)		1.32 (0.69–2.53)	
CRM				0.608
Involved vs noninvolved			1.28 (0.50–3.29)	
Postoperative complications		0.012		
Yes vs no	1.65 (1.12–2.44)			

CRM = circumferential resection margin, HR = hazard ratio, TNM = tumor node metastasis.
*Cox proportional hazards regression model.

postoperative complications can influence oncologic outcomes. Interestingly, there are several reports of inflammation-based predictions of postoperative outcomes in patients with colorectal cancer.[16–19] Ishuzuka et al asserted that the presence of a SIR can be associated with poor oncologic outcomes, because proinflammatory lymphocytes and hypercytokinemia, especially interleukin-6 level elevation, predispose the tumor to further progression, invasion, and metastasis through immunoreactive processes.[16,17] In addition, an elevated Glasgow prognostic score (GPS), an inflammation-based prognostic score, is associated with postoperative mortality.[17] Thus, oncologic outcomes are influenced not only by tumor-related pathologic characteristics but also by SIR-related characteristics. Accordingly, it is theoretically possible that SIR-related postoperative complications affect oncologic outcomes in stage I rectal cancer, which is less influenced by the pathologic factors of the tumor. Currently, several indicators are used to predict mortality in patients, such as the GPS or the Physiology and Operative Severity Score for enUmeration of Mortality and morbidity (POSSUM).[16,20,21] We expect that these indicators will be useful in providing a greater understanding of the effects of surgical complications and their association with oncologic outcomes after surgical procedures.

In this study, the occurrence of postoperative complications was an independent prognostic factor for 5-year disease-free survival. The results of a multivariate analysis showed that postoperative complications had a 1.65 HR for 5-year disease-free survival. In a previous study by Law et al,[10] the occurrence of postoperative complications was an independent factor associated with poor overall survival and a high tumor recurrence rate in colorectal cancer. Because postoperative septic complications and immunosuppression adversely affect outcomes after surgery, the authors suggested that efforts to reduce postoperative complications in colorectal cancer could improve oncologic outcomes. Although our study focused on the outcomes of laparoscopic LAR, the clinical importance of reducing postoperative complications is consistent with the results of the study by Law et al.[10] Our results suggest that careful attention during both surgery and postoperative management to avoid complications is crucial for favorable oncologic outcomes.

Patients with grade III-IV postoperative complications had a lower 5-year disease-free survival rate than those in the NCG and those with grade I-II complications. Patients in the NCG, those with grade I-II complications in the CG, and those with grade III-IV complications in the CG were compared to assess oncologic outcomes according to the severity of postoperative complications. In this study, the rate of anastomotic leakage was 7.0%, comparable with the 8 to 10% rates of anastomotic leakage following laparoscopic procedures reported in previous studies.[2,8] Because anastomotic leakage may lead to extraluminal implantation of tumor cells, there were concerns that it could have a negative effect by diminishing survival through disease upstaging as well as by increasing inflammatory responses, which promote tumor spread.[9,22,23] These findings suggest that surgeons should pay special attention to performing careful surgical procedures in order to prevent postoperative complications.

This study has limitations because it was retrospective in nature and conducted at a single institute. In addition, because open rectal cancer surgeries were excluded, the understanding about the oncologic effects of postoperative complications in rectal cancer surgeries cannot be generalized. In a future study, the impact of postoperative complications on oncologic outcomes in patients undergoing all types of colorectal surgeries should be investigated.

In conclusion, postoperative complications had a negative impact on 5-year disease-free survival after laparoscopic LAR for rectal cancer. The rate of local recurrence in the CG increased more than the NCG. In particular, for stage I cancer,

patients with postoperative complications had poorer oncologic outcomes. Because laparoscopic surgery is preferred in the early stages of rectal cancer, these findings suggest that careful attention is required to avoid postoperative complications following laparoscopic rectal cancer surgery because these could negatively affect long-term oncologic outcomes. Further large-scale, prospective randomized clinical trials are necessary to confirm the present findings.

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